V A P A L O A L T O

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Overview of Severe Sepsis and Septic-Shock

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Contents:

Severe sepsis and resulting organ is the leading worldwide cause of mortality in intensive care units. Both single center studies and national initiatives have shown that mortality of severe sepsis can be reduced by efforts that provide a fast and organized approach to homodynamic stabilization and to the delivery of antibiotics. The VA ICU is doing a number of things to assure that the Veterans are receiving such state of the art care. For this month's issue, an overview of the physiology of severe sepsis and septic shock will be provided, while the next issue will highlight what is being done here and in other parts of the hospital to improve the treatment of severe sepsis.

General concepts

The body's defense against microorganisms is a mixed blessing. Biomolecules that facilitate innate and adaptive immunity have also been linked to impaired function of organs such as the liver, lung and heart, and vasculature. When the inflammatory cascade impairs circulatory function and lowers blood pressure, the problems for these and other end organs are compounded further. The state of malignant inflammation leads to the clinical phenotype of low blood pressure, massive arterial and venous dilation, capillary leak of fluids, and in some cases, myocardial depression. Therapy for septic shock states involves replacing fluid deficits, increasing vascular tone, and if needed, supporting cardiac output with inotropes. This is obviously an oversimplification; any resuscitation scheme requires careful titration of agents, and constant

reappraisal of the entire clinical picture. Too little or too much fluid can be harmful, and "curing a low blood pressure" with a vasopressor while ignoring intravascular volume and cardiac function can be fatal.

Pathophysiology of shock states

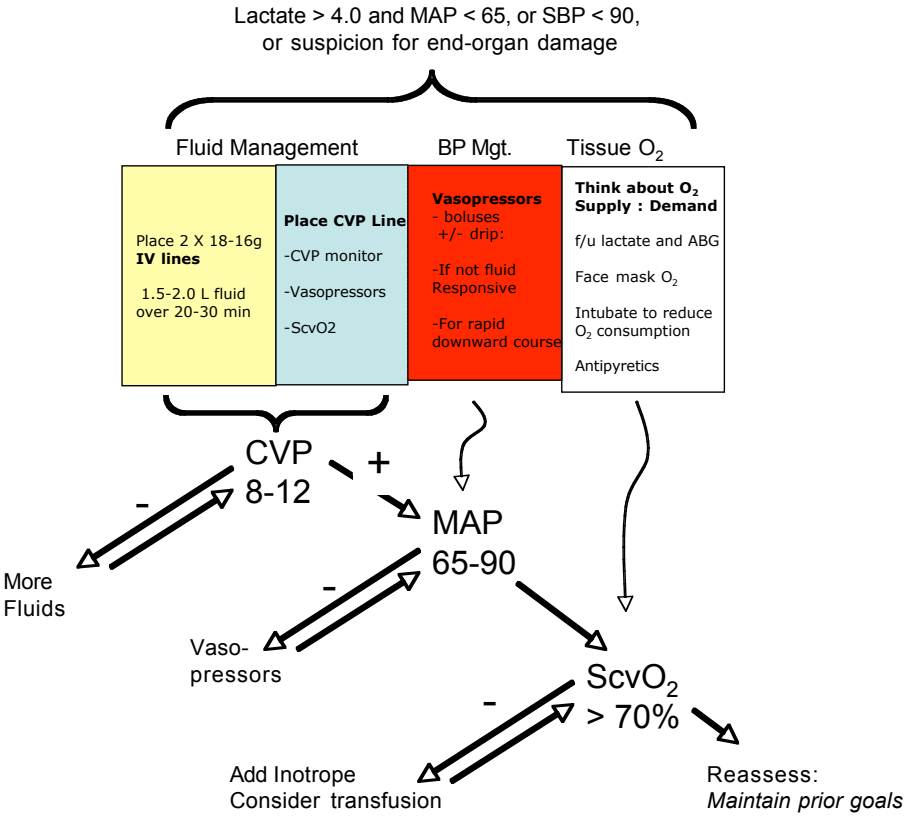
When the circulatory system is compromised, deterioration in end organ function is related to either inadequate supply of oxygen relative to demand, or inadequacy of blood pressure relative to an individual's normal (autoregulatory) range, or both. The following derivations of mean arterial pressure (MAP) and oxygen delivery (DO_2) are pertinent to this discussion:

MAP = CO * SVR

DO_2 = CO * Hb (plus some constants and insignificant factors)

Resuscitation

Given that abnormalities in either blood pressure or oxygen delivery underlie the pathway to organ dysfunction, resuscitation of shock states should center on moving these parameters back towards the patient's normal range. We spend a lot of time discussing and optimizing cardiac output. As one can see from the equations above, interventions that that improve cardiac output create simultaneous improvements in both blood pressure and in oxygen delivery. Indeed, all successful strategies for resuscitation are either explicitly or implicitly based on this principle. One general scheme for resuscitation is presented below; it is a horizontal presentation of the "early goal directed therapy" scheme of Rivers. Think of this as a framework for understanding the pertinent issues rather than "the plan" for all patients.



(resuscitation continued)

While protocols can help guide therapy when you get stuck, it is definitely more important to understand the physiologic principles of resuscitation more than any generalized scheme.

An overview is provided below:

1) Use fluids to improve stroke volume within practical limits
If the patient's cardiac output and blood pressure are highly responsive to fluids---specifically, still on the steep part of the Starling curve—go ahead and fill the ventricle. CVPs in 8-12 have been used to indicate adequate fluid resuscitation in patients early on in the course of severe sepsis. Patients will likely benefit from some individualization of CVP goals based on bedside echocardiography. At some point, the BP no longer responds to fluids. If further increases in BP are deemed necessary, attention should shift towards whether an inotrope or vasopressor is also needed.

2) If fluids have been used to improve stroke volume and the cardiac output is still not sufficient to meet metabolic demands, improve ventricular function with inotropic agents. In the older days, the cardiac indices were measured with PA catheters and pushed up to very high levels (C.I. > 4.5) with aggressive use of fluids and inotropes. Studies on septic patients using this approach, however, failed to demonstrate any better survival resulting from this strategy. Echo and mixed venous oxygen saturation are now more commonly used to gain information about cardiac function and the oxygen supply/ demand relationship. This shift represents a more appropriate focus of resuscitation goals on function and metabolism rather than on a set of numerical values that might exceed what is needed, or that may be greater than what a patient can actually achieve. Accordingly, if the delivery of oxygen is sufficient to meet demands (as evidenced by a normal mixed venous O_2 saturation of about 70%), the heart probably does not need to be filled or pushed further.

3) If the blood pressure is still inadequate after optimizing cardiac function, use vasopressors to increase BP. The problem with this statement is the suggestion that you need to titrate fluids and inotropes, and do a number of studies *before* improving a patient's blood pressure. While all clinical algorithms present resuscitation in these terms, this is not practical. In reality, what we end up doing is *carefully using* pressors fairly early on to normalize BP while we are placing lines, giving fluids, evaluating cardiac function, etc. Vasopressor doses are decreased while fluid resuscitation takes place. When we are lucky, pressors are not needed after fluid resuscitation, but in most cases, we do have to use vasopressors for a day or two. Nonetheless, if the initial exam suggests massive vasodilation, there is nothing wrong with working on BP at the same time as fluid optimization takes place. The huge error to avoid is assuming that the patient is resuscitated just because the BP is improved with a vasopressor.

Summary

The hemodynamic management of severe sepsis and septic shock is driven by a bedside evaluation of fluid

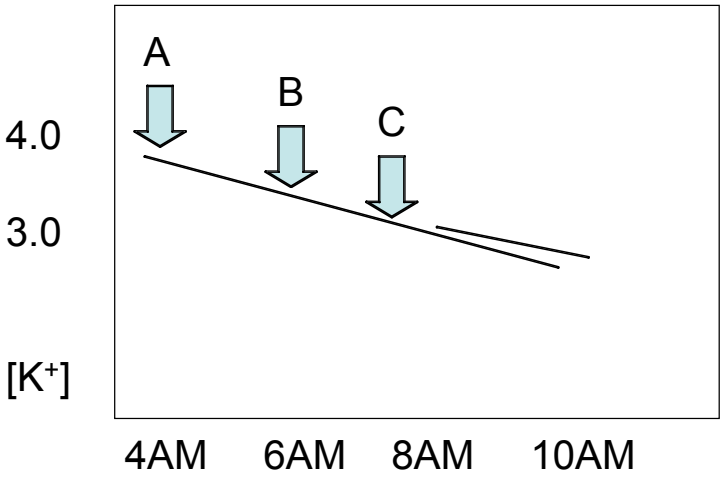
responsiveness, adequacy of contractility and vascular resistance. The efficacy of any intervention will be lost if too much time elapses between the onset organ dysfunction (especially hypotension), and resuscitation. Rapid administration of antibiotics, and urgent hemodynamic optimization are linked with a better survival of sepsis. The latter are two areas where the ICU needs to reach out to the rest of the hospital-- first to provide education regarding factors that influence outcome, and secondly, to help assure access to the resources that can provide this difference.

Potassium Replacement Scales--Helpful or Harmful??

Janell Kobayashi, Pharm D

Hypokalemia is a common and preventable electrolyte disorder in our ICU. If untreated or under-treated, hypokalemia can lead to muscle weakness, cardiac arrhythmias, and EKG changes. It is important to be proactive rather than reactive when replacing potassium in order to prevent these complications. Most healthcare workers know the causes of hypokalemia (increased elimination, decreased intake, and increased uptake into cells), but they do not realize that the potassium replacement scale alone is often not enough to prevent or treat hypokalemia. Most practitioners mistakenly rely on the replacement scale as the only source of repletion. This is often not sufficient in patients with ongoing losses. Many practitioners replace potassium too conservatively especially in patients with high ongoing losses, as in patients on diuretics.

The diagram below illustrates what we commonly see: a borderline low/ normal potassium level is present at 4AM at the time of morning phlebotomy. By 6AM, the result is available and acted upon by an order or scale that triggers the administration of 10-20 meq IV by 7-8AM. Throughout this time, the serum potassium is in a state of constant decline, sometimes hitting dangerous lows. When the infusion begins, there is a drop in the loss rate (upper line), but in most instances of moderate to high urine output, the serum level is not corrected by the small amount administered. The ideal course involves a better match between intake and losses.



One can make a very accurate assessment of potassium losses by looking at the urinary K+ concentration and multiplying by the total urine output for the day. Typical losses are in the range of 100-200 mEq/ day for non-dialysis patients. Here are some helpful hints for preventing and treating hypokalemia:

- Find and correct the cause, if possible.
- Look at the total daily IV and PO potassium replacement trends.

- If a patient with hypokalemia is consistently requiring 100 mEq/day, order at least 100 mEq daily in divided doses in addition to the scale.
- If you are diuresing a patient, you should give enteral replacements; if not, you will likely end up giving back a lot of volume with IV potsssium
- Maximum IV dose = 20 mEq/hr (central IV) and 10 mEq/hr (peripheral IV).
- Limit single oral doses to 40 mEq or less to decrease GI irritation, nausea and vomiting.
- Remember that potassium will be replaced with the replacement scale only after potassium is checked. Once daily labs will result in the potassium only being replaced once during the day.

New Faces in the ICU

Bethany Eytchison, RN

Hello there! I have been a part of the MSICU family since May 2009. I recently graduated from DeAnza College's Nursing Program in December of 2008. Getting hired in the Intensive Care setting straight out of school has been such an amazing adventure and I feel so privileged to be working with such great staff.

I grew up in California and currently live in San Jose. I have a 2 year old black pug named Pteradactyl, yes like the dinosaur. On my days off I try to spend time outdoors. I love to play soccer or volleyball, take Pteradactyl to the beach, rock climb or just be lazy and catch up on much needed sleep!

I really do enjoy working here and am very excited to be apart of the team. Almost one year down and so many more to go!

Tricia Martinez, RN

Hi there! I am a December 2008 graduate from San Jose State University's School of Nursing. I started working as a New Grad in the MSICU in March, 2009. However, I have been employed by the VA Palo Alto since July 2007. While in nursing school, I worked in the MSICU as a Nurse Assistant/Student Nurse Technician. From May to December 2008 I had the opportunity to work as a VALOR student in the MSICU as well, where I was able to care for patients under the supervision of a preceptor. I feel like I have learned so much from working on the unit and it has only helped me transition from student to nurse.

When I'm not working, I love hanging out with my family and friends. I also love to dance, cook, bake, knit, watch movies, go to the beach or snowboard when the weather is appropriate. And everyone on the unit pretty much knows about my obsession with Twilight! I love working in the MSICU with the amazing staff. I may be biased, but I think we have the most awesome ICU nurses! I have learned so much from them, and I look forward to working with all of them for a long time.

Preventing Adverse Consequences of Ventilation During CPR

T. Kyle Harrison, MD

"First do no harm" is one of the cardinal tenets of health care. However in the history of medicine there have been innumerable examples where health care providers have attempted to help their patients only to find with new information that they were actually harming them. One such example is in the over ventilation of cardiac arrest patients. Since cardiopulmonary resuscitation (CPR) was first described, it has always relied on positive pressure ventilation. The problem arises when the positive pressure ventilation competes and reduces the effectiveness of the chest compressions.

Effective CPR requires the creation of negative intrathoracic pressure created by the passive recoil of the chest following a compression. Positive pressure ventilation obliterates this negative intrathoracic pressure and effectively negates the compressions. To be effective CPR must be performed at a rate of 100 compressions per minute; therefore ventilation rates greater than 12 will dramatically reduce the effectiveness of CPR potentially to the point that the patient will be unresuscitable. In addition to the rate, the length of the breath also matters. Giving a slow long breath will maintain an increased intrathoracic pressure and will prevent the negative intrathoracic pressure needed for effective chest compressions. In an interesting study of paramedics responding to cardiac arrest calls, investigators showed that the average ventilation rate during CPR was 37 breaths per minute. With extensive retraining of the EMS personal to maintain a rate of 12 bpm, the paramedics reduced the ventilation rate on cardiac arrest calls to 22 bpm but it was discovered that they were giving longer breaths effectively creating the same physiology as if they were giving the increased breaths.

Our experience with mock codes here at the VA supports these findings with code responders typically ventilating the patient in the high 20's. Even with

appropriate education, there is a tendency to over ventilate--likely due to the stress of the environment as well as a lack of appreciation of true ventilation rates (I can personally attest to this because I often finding myself over ventilating patients even when I know how damaging it can be). Fortunately there are devices that can assist in monitoring the patient for over ventilation. Some utilize the pads for the defibrillator to measure respiratory rate and others give visual or verbal cues to maintain the appropriate ventilatory rate. One exciting new device that we will soon start using for cardiac arrest calls is the ResQPOD an impedance threshold device (ITD, see below).

The ResQPOD connects to the patient's airway either an ET tube or to the mask of an Ambu bag and has a one way valve that and allows for passive exhalation but prevents air entry into the lungs during the passive recoil of the chest after a compression. This allows for a marked improvement in the generation of negative intrathoracic pressure (-3 to -8 mmHg with CPR +ITD compared to 0 to -2 mmHg with CPR and no ventilation) augmenting the each compression. This augmentation doubles systolic blood flow during CPR (45mmHg with standard CPR vs. 85 mmHg CPR +ITD). The device also has a visual timing cue for ventilation helping to prevent hyperventilation.

Clinical studies have been encouraging with a dramatic improvement in resuscitation rates and most importantly improvement in long-term recovery without neurological injury (25% CPR only vs. 60% with ITD +CPR). If we as code team members all strive to deliver good and effective CPR and prevent the over ventilation of the cardiac arrest patient, then we can give our patients their best chance at surviving a cardiac arrest.

(http://www.advancedcirculatory.com)

Random Notes

Wanted!! Articles pertaining to the MSICU, critical care, veterans, etc. that would be of interest to the multiple disciplines practicing in the VA ICU. Controversies are especially welcome Send to: geoffrey.lighthall@va.gov

Errata: In v.1, Fred Rice's last name was incorrectly spelled Tice. The insult has been repaid in full!!